AMENDMENTS TO THE CLAIMS

1-54. (Canceled)

55. (Currently amended) A method comprising:

a) generating *in silico* virtual compounds according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof, wherein synthetic compounds corresponding to said virtual compounds modulate the expression of [a]said target nucleic acid sequence;

b) synthesizing compounds corresponding to at least some of said virtual compounds; and

c) robotically assaying said synthetic compounds for one or more desired physical, chemical or biological properties by computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

56. (Currently amended) A method comprising:

evaluating *in silico* a plurality of virtual compounds according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof; and

robotically assaying a plurality of synthetic compounds corresponding to at least some of said virtual compounds for one or more desired physical, chemical or biological properties by

computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

57. (Canceled)

58. (Currently amended) A method comprising:

generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof; and

robotically assaying a plurality of synthetic compounds having at least some of said nucleobase sequences for one or more desired physical, chemical or biological properties by computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

59. (Currently amended) A method comprising:

evaluating *in silico* a plurality of virtual compounds according to defined criteria, wherein said defined criteria [is]comprise a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof; and

robotically assaying a plurality of synthetic compounds corresponding to at least some of said virtual compounds for one or more desired physical, chemical or biological properties.

60. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other [criteria]criterion selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof, wherein said oligonucleotides modulate the expression of [a]said target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion[defined criteria]; and

c) robotically assaying a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled polymerase chain reaction or by computer controlled enzyme-linked immunosorbent assay.

61. (Previously presented) The method of claim 60 wherein said target nucleic acid sequence is genomic DNA, cDNA, product of a polymerase chain reaction, expressed sequence tag, mRNA or structural RNA.

62. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) robotically synthesizing a plurality of synthetic oligonucleotides having at least some of said nucleobase sequences; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

63. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) evaluating *in silico* a plurality of virtual oligonucleotides according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

64. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion [criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof];

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

d) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

65. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from target accessibility, targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) choosing an oligonucleotide chemistry;

c) robotically synthesizing a set of synthetic oligonucleotides having said nucleobase sequences of step a) and said oligonucleotide chemistry of step b);

d) robotically assaying said set of synthetic oligonucleotides of step c) for a physical, chemical or biological activity by computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay; and

e) selecting a subset of said set of synthetic oligonucleotides of step c) having a desired level of physical, chemical or biological activity in order to generate said set of compounds.

66. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) choosing an oligonucleotide chemistry;

c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) and the oligonucleotide chemistry of b) according to said thermodynamic property and said at least one other criterion, [criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof,]and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

d) robotically synthesizing a set of synthetic oligonucleotides having said preferred nucleobase sequences of step c) and said oligonucleotide chemistry of step b);

e) robotically assaying said set of synthetic oligonucleotides of step (d) for a physical, chemical or biological activity by computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay; and

f) selecting a subset of said set of synthetic oligonucleotides of step d) having a desired level of physical, chemical or biological activity in order to generate said set of oligonucleotides.

67. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof, wherein said oligonucleotides modulate the expression of [a]said target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion[criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof]; and

c) robotically assaying a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties.

68. (Previously presented) The method of claim 67 wherein said target nucleic acid sequence is genomic DNA, cDNA, product of a polymerase chain reaction, expressed sequence tag, mRNA or structural RNA.

69. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria, wherein said defined criteria [is]comprise a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target

nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

70. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion[criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to said target nucleic acid sequence, and combinations thereof];

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

d) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

71. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) choosing an oligonucleotide chemistry;

c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) and the oligonucleotide chemistry of b) according to said thermodynamic property and said at least one other criterion, [criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof,]and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

d) robotically synthesizing a set of synthetic oligonucleotides having said preferred nucleobase sequences of step c) and said oligonucleotide chemistry of step b);

e) robotically assaying said set of synthetic oligonucleotides of step (d) for a physical, chemical or biological activity; and

f) selecting a subset of said set of synthetic oligonucleotides of step d) having a desired level of physical, chemical or biological activity in order to generate said set of oligonucleotides.

72. (Currently amended) A method comprising:

evaluating *in silico* a plurality of virtual oligonucleotides according to a thermodynamic property, and at least one other criterion [criteria]selected from [target accessibility,]targeting to

functional regions of a target nucleic acid sequence, or]uniform distribution to said target nucleic acid sequence, and combinations thereof; and

robotically assaying a plurality of synthetic oligonucleotides corresponding to least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

73. (Canceled)

74. (Currently amended) A method comprising:

generating a library of nucleobase sequences *in silico* according to a thermodynamic property, and at least one other criterion criteria selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, or]uniform distribution to said target nucleic acid sequence, and combinations thereof; and

robotically assaying a plurality of synthetic oligonucleotides having said nucleobase sequences for one or more desired physical, chemical or biological properties by computer controlled polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

75. (Currently amended) A method comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion[criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof]; and

c) robotically assaying a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled polymerase chain reaction or by computer controlled enzyme-linked immunosorbent assay.

76. (Previously presented) The method of claim 75 wherein said nucleic acid sequence genomic DNA, cDNA, product of a polymerase chain reaction, expressed sequence tag, mRNA or structural RNA.

77. (Canceled)

78. (Currently amended) A method comprising:

a) evaluating *in silico* a plurality of virtual oligonucleotides according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

79. (Currently amended) A method comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion;[criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof,]

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to least some of said plurality of virtual oligonucleotides; and

d) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

80. (Currently amended) A method comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) choosing an oligonucleotide chemistry;

c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion[criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence], and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

d) robotically synthesizing a set of synthetic oligonucleotides having said preferred nucleobase sequences of step b) and said oligonucleotide chemistry of step c);

e) robotically assaying said set of synthetic oligonucleotides of step d) for a physical, chemical or biological activity; and

f) selecting a subset of said set of oligonucleotides of step d) having a desired level of physical, chemical or biological activity.

81. (Currently amended) A method comprising:

evaluating *in silico* a plurality of virtual oligonucleotides according to a thermodynamic property and at least one other criterion criteria selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof; and

robotically assaying a plurality of synthetic oligonucleotides corresponding to least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties.

82. (Currently amended) A method comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion; [criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof,]and

c) robotically assaying a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties.

83. (Previously presented) The method of claim 82 wherein said nucleic acid sequence is genomic DNA, cDNA, product of a polymerase chain reaction, expressed sequence tag, mRNA or structural RNA.

84. (Canceled)

85. (Currently amended) A method comprising:

a) evaluating *in silico* a plurality of virtual oligonucleotides according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

86. (Currently amended) A method comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;[,]

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and at said least one other criterion[criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof];

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to least some of said plurality of virtual oligonucleotides; and

d) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

87. (Currently amended) A method comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to

functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) choosing an oligonucleotide chemistry;

c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion[criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof, and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences];

d) robotically synthesizing a set of synthetic oligonucleotides having said preferred nucleobase sequences of step b) and said oligonucleotide chemistry of step c);

e) robotically assaying said set of synthetic oligonucleotides of step d) for a physical, chemical or biological activity; and

f) selecting a subset of said set of oligonucleotides of step d) having a desired level of physical, chemical or biological activity.

88-98. (Canceled)

99. (Currently amended) A method comprising:

evaluating *in silico* a plurality of virtual compounds according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to target nucleic acid sequence, and combinations thereof;[,] and

robotically synthesizing a plurality of synthetic compounds corresponding to said plurality of virtual compounds.

100. (Currently amended) A method of generating a set of oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion; [criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof,]and

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides.

101. (Currently amended) A method of preparing oligonucleotides comprising:

evaluating *in silico* a plurality of virtual oligonucleotides according to a thermodynamic property and at least one other criterion [criteria]selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof; and

robotically synthesizing a plurality of synthetic oligonucleotides corresponding to least some of said virtual oligonucleotides.

102. (Currently amended) A method of preparing oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to a thermodynamic property and at least one other criterion criteria selected from [target accessibility,]targeting to functional regions of a target nucleic acid sequence, [or]uniform distribution to said target nucleic acid sequence, and combinations thereof;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to said thermodynamic property and said at least one other criterion[criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof]; and

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides.

103. (Canceled)